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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,668	03/19/2004	William A. Zoghbi	HO-P02680US1	8004

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EXAMINER	
BORGEEST, CHRISTINA M	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/804,668	ZOGHBI ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *18 May 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the species BNP and treadmill or bicycle test in the reply filed on 28 February 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-44 are pending. Claims 15-17, 37-39 are drawn to a nonelected species, however, upon further consideration, the examiner has decided to ***withdraw the species requirement*** because inducing pharmacological stress in lieu of exercise induced stress is an obvious variation. Claims 1-44 are under examination.

Specification

The abstract of the disclosure is objected to because it contains the phrase "said cardiac stress". Abstracts should be written in plain English and be free of legal phraseology. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because it contains the language "said cardiac stress". Correction is required. See MPEP § 608.01(b).

Information Disclosure Statement

The information disclosure statement filed 18 May 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Citations BA, CC, CD, CE, CF, CG, CH, CK, CL, CM, CO, CQ, CR, CS, CT, CU, CV, CX, CZ, CA1, CB1 have abstracts only, but not a full copy of the application. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 14, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 34, 36, 40, 41, 42, 43, 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Marumoto et al. (citation CP on Applicants' Information Disclosure

Sheet). The claims recite a method of detecting coronary artery disease (CAD) in a human with no known history of a previous myocardial infarction, but with at least one cardiac risk factor as recited in claim 8, comprising measuring BNP in the human by immunoassay at baseline, inducing cardiac stress via exercise testing (treadmill or bicycle test), wherein a single photon emission computed tomography test is co-administered during induction of cardiac stress, measuring BNP about 10-15 minutes post-cardiac stress, calculating a relative change in the marker related to BNP wherein CAD is detected if the relative change after cardiac stress is greater than predetermined clinically effective values. Marumoto et al. teach a method of measuring BNP by radioimmunoassay at baseline (*i.e.*, a predetermined clinically effective threshold value—no other predetermined clinically effective threshold value is defined in the specification) in humans suspected of having CAD with at least one of the risk factors of CAD as recited claim 8 (*e.g.* age greater than 35 years), but with no history of myocardial infarction, inducing cardiac stress via exercise testing and co-administering a single photon emission computed tomography test, measuring BNP 30 minutes post cardiac stress, and correlating BNP measurements with severity score in patients with chest pain, wherein BNP levels reflected acute myocardial ischemia in patients with chest pain (see p. 551-553, entire section under Materials and Methods; p. 554, Figure 2 and left column, 4th paragraph). Myocardial ischemia represents a pathological development in the course of coronary artery disease, thus inherently represents a stage in CAD. Applicants do not define the "predetermined clinically effective threshold value" in the specification as a number, but rather, in broad terms to indicate that the

value may be adjusted depending upon whether one is seeking greater sensitivity or specificity of the clinical test (see [0058]). No number value is given, thus the resting BNP levels recorded in Marumoto et al. could serve as a threshold value. Marumoto et al. state that BNP was measured 30 minutes after cardiac stress was induced, and claim 5 recites "about 10-15 minutes post cardiac stress". Because of the use of open language ("about"), Marumoto et al. read on "about 10-15 minutes". Claims 18-22 recite the method of claim 1, wherein: the relative change in the marker related to BNP is from about 10% (claim 18) 10% to about 400% (claim 19), at least about 1% per minute of exercise (claim 20), at least about 5% per minute of exercise (claim 21) and about 5% to about 27% per minute of exercise (claim 22). Because Marumoto et al. teach the same method steps as recited in the instant claim 1, the limitations recited in claims 18-22 would by necessity inherently be met by Marumoto et al., although they are silent with respect to the specific values taught in the claim. Marumoto et al. teach the same method as Applicants, in the same population of patients, and the results of Marumoto et al. predicted severity of CAD. Marumoto et al. state on p. 555, middle of the 1st paragraph, that plasma BNP levels at peak exercise may reflect the severity of myocardial ischemia, thus the method as taught could be used to diagnose CAD and the conclusions drawn by Marumoto et al. (exercising BNP levels are higher in those individuals with chest pain) could be used in risk stratification.

Thus the claims do not contribute anything over the prior art teaching of Marumoto et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 13, 23 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marumoto et al as applied to claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 14, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 34, 36, 40, 41, 42, 43, 44 above, and further in view of Tavel (Tavel, Chest. 2001; 119: 907-925). The teachings of Marumoto et al. are discussed above. Marumoto do not teach co-administration of a stress echocardiography test during induced cardiac stress. Tavel teaches the coadministration of a stress echocardiography test during induced cardiac stress, (see whole document). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Marumoto et al. by co-

administering a stress echocardiography test, as taught in Tavel because according to Tavel, "exercise testing with ECG monitoring remains a cornerstone of cardiovascular evaluation" (p. 919, right column, 3rd paragraph). The person of ordinary skill in the art would have been motivated to use ECG monitoring because it is already standard in the art, and for this reason as well, the person of ordinary skill in the art could have reasonably expected success. Thus the claims do not contribute anything non-obvious over the prior art.

Claims 1, 9, 10, 23, 31, 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marumoto et al. as applied to claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 14, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 34, 36, 40, 41, 42, 43, 44 above, and further in view of Tavel (Chest, 2001; 119: 907-925). The teachings of Maruomoto et al. are discussed above under Rejections under 35 USC 102. Marumoto do not teach the type of exercise testing used. Tavel teaches that treadmill or bicycle exercise testing are obvious variants (see p. 907, right column, 2nd paragraph). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Marumoto et al. by using either bicycle or treadmill testing, as taught in Tavel because states that either type of test can be used. The person of ordinary skill in the art would have been motivated to use either test because they are the most commonly performed stress tests (p. 907, right column, 2nd paragraph). Furthermore, the person of ordinary skill in the art could have reasonably

expected success for the same reasons. Thus the claims do not contribute anything non-obvious over the prior art.

Claims 1, 15, 16, 17, 23, 37, 38, 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marumoto et al as applied to claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 14, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 34, 36, 40, 41, 42, 43, 44 above, and further in view of Raza et al. (Inter J Cardio. 2001; 31: 157-167). The teachings of Marumoto et al. are discussed above under Rejections under 35 USC 102. Marumoto et al. do not teach using pharmacological agents in lieu of exercise stress testing. Raza et al. teach the use of pharmacological stress induction (*e.g.*, dobutamine or adenosine). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Raza et al. by administering dobutamine or adenosine, as taught in Raza et al. because pharmacologic agents can be used in lieu of exercise in stress testing in cases where the patients are not able to exercise for medical reasons (p. 158, left column, 1st paragraph). The person of ordinary skill in the art would have been motivated to administer pharmacologic agents in cases where patients are too ill to perform the exercise test adequately. Furthermore, the person of ordinary skill in the art could have reasonably expected success because such methods of administering stress tests are old in the art and have a track record of success. Thus the claims do not contribute anything non-obvious over the prior art.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Goodman and Kirwan (Sports Med. 2001: 31: 235-47) is presented to show that myocardial ischemia represents a pathological development in the course of coronary artery disease, thus represents a stage in CAD (see abstract).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

Christina Borgeest, Ph.D.

ELIZABETH KEMMERER
PRIMARY EXAMINER